Review 1: "Adverse effects and antibody titers in response to the BNT162b2 mRNA COVID-19 vaccine in a prospective study of healthcare workers"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

The research in this article is very meaningful, but there are still some issues that need to be explored in-depth.

1. The article lacks a PBS blank control group, and thus could not explain whether the adverse reaction is caused by the vaccination method or the vaccine antigen.
2. Compared with primary immunization, the adverse reactions increased after the booster immunization, but the manuscript does not explain why it increased. Regarding the increase of adverse reactions and antibody titers after booster immunity, does booster immunity induce a stronger immune response, thus enhancing adverse reactions and antibody titers?
3. As mentioned in the article, there is no relationship between antibody titers and adverse reactions, and there may be a correlation between T cell reactions and adverse reactions. The author should provide references for this statement in the discussion.
4. Whether the participants drink alcohol or use other drugs after vaccination also has an impact on the adverse reactions of the vaccine.
5. The adverse reactions shown in the article have more inflammatory reactions, such as redness and swelling at the injection site, whole-body fever, lymphadenopathy, etc. The article also mentions the role of IL-6 and other inflammatory factors in this process. Are there test results for these cytokines to further explain how the adverse reactions are produced?